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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,875	12/09/2003	Paul D. Thomas	9692-000029	9480

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EXAMINER	
NEGIN, RUSSELL SCOTT	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 07/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,875	THOMAS ET AL.	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *11-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I (Claims 1-10) in the reply filed on 17 May 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 11-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 17 May 2006.

Specification

The disclosure is objected to because of the following informalities: The second line on page 5 has a spelling error in the word "involcves."

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Ladunga [Current Opinion in Biotechnology, 2000, volume 11, pages 13-18].

Claims 1 and 8 state:

1. A browsable database system for use with biological information, comprising; at least one datastore of biological sequence data, including at least one of gene sequence data and protein sequence data; an ontology of categories of biological functions mapped to statistical models trained on families of biological sequences related to the biological functions; an input receptive of at least one user selection indicating a biological function of said ontology; a recognizer adapted to identify multiple alignments of biological sequence data based on said sequence datastore and a statistical model related to a function indicated by the user selection; and an output adapted to communicate the multiple alignments to a user providing the user selection.

8. The system of claim 1, further comprising an input receptive of a user-defined sequence, wherein said recognizer is adapted to select functional categories and subcategories related to statistical models achieving high scores respective of the user-defined sequence.

The article of Ladunga, entitled, "Large-scale predictions of secretory proteins from mammalian genomic and EST sequences," explain on column 2 of page 13, lines 5-10, "After briefly discussing the molecular anatomy of SPs [secretory proteins] and the experimental tools for the identification of secretory proteins, we cover their computational predictions by traditional and machine learning tools, with specific reference to the analysis of uncovered sequences and the predictions of cell-to-cell and intracellular signaling domains." Figure 1 shows browsable data showing tripartite organization and the lack of conservation in 2,532 eukaryotic signal peptides.

Ladunga shows a scoring procedure on page 15, column 1, lines 30-39, which state, "Machine learning finds locally or globally optimal weights for linear or nonlinear separation between classes of objects. Machine learning, like positional weight matrices, utilizes certain feature, including the occurrence of a residues, tripeptide, nucleotide at a given position, hydropathy of a segment, structural conformation and so

on. The score for a query sequence of segment is defined as the weighted sum of the values of the features, for example, the weighted sum of the residues at the positions analyzed."

Ladunga continues in column 2 of page 15 by explaining how neural networks and Hidden Markov Models can be used to aid in sequence identification and prediction. Ladunga continues by stating the last two lines of column 2 on page 15 and the first paragraph of column 1 on page 16, "Generalizations from a few thousand training sequences to the astronomic number of possible SPs can be improved by estimating functionally relevant physico-chemical and biological parameters from raw sequence data.... certain physical, chemical, and steric properties of the residues can be diagnostic for the functionality of an SP." In effect, mapping functional properties of the peptides to the models described above can be useful in limiting the possible number of sequences in alignment procedures.

Input procedures are described in the last paragraph of column 1 on page 16 of Ladunga, which states, "Atypical entries, such as the SPs of antifreeze glycoproteins with no H region, and erroneous classifications in the training sets may introduce heavy bias into machine learning." In this case, the input protein has the function of acting as an antifreeze.

The section of Ladunga in column 2 of page 16 describes, "Prediction from ESTs and genomic sequences" and states in the last sentence of the section, "To improve the assessments of cellular localization, biochemical functions and pathological roles,

domains are represented as single sequences, gapped multiple alignments, and HMMs [Hidden Markov Models], searchable by BLAST, Searchwise, and HMMER."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ladunga in view of Genaissance [WIPO WO 01/01218].

Claims 1-7 and 9 state:

1. A browsable database system for use with biological information, comprising; at least one datastore of biological sequence data, including at least one of gene sequence data and protein sequence data; an ontology of categories of biological functions mapped to statistical models trained on families of biological sequences related to the biological functions; an input receptive of at least one user selection indicating a biological function of said ontology; a recognizer adapted to identify multiple alignments of biological sequence data based on said sequence datastore and a statistical model related to a function indicated by the user selection; and an output adapted to communicate the multiple alignments to a user providing the user selection.

2. The system of claim 1, further comprising at least one datastore of curated philogenetic trees organized into families of sequences based on global sequence similarity, wherein the families are divided into subfamilies according to sequence function and the families and subfamilies are mapped to appropriate statistical models.

3. The system of claim 2, further comprising an output communicating contents of the philogenetic trees to the user in accordance with user navigation selections.

4. The system of claim 2, further comprising a text searcher receptive of user defined text and adapted to select families and subfamilies of the philogenetic trees by matching the text to contents of the philogenetic trees.

5. The system of claim 2, further comprising an input receptive of a user-defined sequence, wherein said recognizer is adapted to select families and subfamilies related to statistical models achieving high scores respective of the user-defined sequence.

6. The system of claim 1, further comprising an output communicating contents of the ontology to the user in accordance with user navigation selections.

7. The system of claim 1, further comprising a text searcher receptive of user defined text and adapted to select functional categories and subcategories by matching the text to contents of the ontology.

9. The system of claim 1, further comprising an input receptive of database selections, wherein said recognizer is adapted to identify sequences in a subset of multiple sequence datastores based on the database selections.

The article of Ladunga, entitled, "Large-scale predictions of secretory proteins from mammalian genomic and EST sequences," explain on column 2 of page 13, lines 5-10, "After briefly discussing the molecular anatomy of SPs [secretory proteins] and the experimental tools for the identification of secretory proteins, we cover their computational predictions by traditional and machine learning tools, with specific reference to the analysis of uncovered sequences and the predictions of cell-to-cell and intracellular signaling domains." Figure 1 shows browsable data showing tripartite organization and the lack of conservation in 2,532 eukaryotic signal peptides.

Ladunga shows a scoring procedure on page 15, column 1, lines 30-39, which state, "Machine learning finds locally or globally optimal weights for linear or nonlinear separation between classes of objects. Machine learning, like positional weight matrices, utilizes certain feature, including the occurrence of a residues, tripeptide, nucleotide at a given position, hydropathy of a segment, structural conformation and so on. The score for a query sequence of segment is defined as the weighted sum of the

values of the features, for example, the weighted sum of the residues at the positions analyzed."

Ladunga continues in column 2 of page 15 by explaining how neural networks and Hidden Markov Models can be used to aid in sequence identification and prediction. Ladunga continues by stating the last two lines of column 2 on page 15 and the first paragraph of column 1 on page 16, "Generalizations from a few thousand training sequences to the astronomic number of possible SPs can be improved by estimating functionally relevant physico-chemical and biological parameters from raw sequence data.... certain physical, chemical, and steric properties of the residues can be diagnostic for the functionality of an SP." In effect, mapping functional properties of the peptides to the models described above can be useful in limiting the possible number of sequences in alignment procedures.

Input procedures are described in the last paragraph of column 1 on page 16 of Ladunga, which states, "Atypical entries, such as the SPs of antifreeze glycoproteins with no H region, and erroneous classifications in the training sets may introduce heavy bias into machine learning." In this case, the input protein has the function of acting as an antifreeze.

The section of Ladunga in column 2 of page 16 describes, "Prediction from ESTs and genomic sequences" and states in the last sentence of the section, "To improve the assessments of cellular localization, biochemical functions and pathological roles, domains are represented as single sequences, gapped multiple alignments, and HMMs [Hidden Markov Models], searchable by BLAST, Serarchwise, and HMMER."

However, Ladunga does not show phylogenetic trees or several required features of the browsable database claimed in instant set of claims.

Genaissance illustrates phylogenetic trees in Figure 35 of the document where sequences have been divided into families and these families have been divided into subfamilies based on the separate hosts in which the gene sequences function. Figure 35 also illustrates computer characteristics of the browser that are required by the instant set of claims (i.e. navigation, text searching).

Figures 3, 4a and 8 elaborate on input receptive to database selection.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify Ladunga in view of Genaissance to result in the instantly claimed invention because while Ladunga teaches the method of using models to limit possible secretory protein alignments based on function, Genaissance uses these sequences and further divides them into family trees based on functions for the purpose of better understanding of sequence relationships.

Claims 1 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ladunga in view of Jay [USPAT 6,960,562 B2].

Claims 1 and 10 state:

1. A browsable database system for use with biological information, comprising; at least one datastore of biological sequence data, including at least one of gene sequence data and protein sequence data; an ontology of categories of biological functions mapped to statistical models trained on families of biological sequences related to the biological functions; an input receptive of at least one user selection indicating a biological function of said ontology; a recognizer adapted to identify multiple alignments of biological sequence data based on said sequence datastore and a statistical model related to a function indicated by the user selection; and an output adapted to communicate the multiple alignments to a user providing the user selection.

10. The system of claim 1, further comprising an input receptive of a user selection of a Boolean operator, wherein said recognizer is adapted to identify the multiple alignments in accordance with the Boolean operator.

The article of Ladunga, entitled, "Large-scale predictions of secretory proteins from mammalian genomic and EST sequences," explain on column 2 of page 13, lines 5-10, "After briefly discussing the molecular anatomy of SPs [secretory proteins] and the experimental tools for the identification of secretory proteins, we cover their computational predictions by traditional and machine learning tools, with specific reference to the analysis of uncovered sequences and the predictions of cell-to-cell and intracellular signaling domains." Figure 1 shows browsable data showing tripartite organization and the lack of conservation in 2,532 eukaryotic signal peptides.

Ladunga shows a scoring procedure on page 15, column 1, lines 30-39, which state, "Machine learning finds locally or globally optimal weights for linear or nonlinear separation between classes of objects. Machine learning, like positional weight matrices, utilizes certain feature, including the occurrence of a residues, tripeptide, nucleotide at a given position, hydropathy of a segment, structural conformation and so on. The score for a query sequence of segment is defined as the weighted sum of the values of the features, for example, the weighted sum of the residues at the positions analyzed."

Ladunga continues in column 2 of page 15 by explaining how neural networks and Hidden Markov Models can be used to aid in sequence identification and prediction. Ladunga continues by stating the last two lines of column 2 on page 15 and the first paragraph of column 1 on page 16, "Generalizations from a few thousand training

sequences to the astronomic number of possible SPs can be improved by estimating functionally relevant physico-chemical and biological parameters from raw sequence data.... certain physical, chemical, and steric properties of the residues can be diagnostic for the functionality of an SP." In effect, mapping functional properties of the peptides to the models described above can be useful in limiting the possible number of sequences in alignment procedures.

Input procedures are described in the last paragraph of column 1 on page 16 of Ladunga, which states, "Atypical entries, such as the SPs of antifreeze glycoproteins with no H region, and erroneous classifications in the training sets may introduce heavy bias into machine learning." In this case, the input protein has the function of acting as an antifreeze.

The section of Ladunga in column 2 of page 16 describes, "Prediction from ESTs and genomic sequences" and states in the last sentence of the section, "To improve the assessments of cellular localization, biochemical functions and pathological roles, domains are represented as single sequences, gapped multiple alignments, and HMMs [Hidden Markov Models], searchable by BLAST, Serarchwise, and HMMER."

However, Ladunga does not show Boolean searches as claimed in instant claims.

In the patent of Jay, entitled, "Tribonectin in polypeptides and uses thereof," Jay claims in column 36, lines 6-8, Jay states, "A Boolean search of Online Mendelian Inheritance in Man (OMIM) revealed one arthritic disease which has been genetically mapped to the same locus."

It would have been obvious to someone of ordinary skill at the time of the instant invention to modify Ladunga in view of Jay to result in the instantly claimed invention because while Ladunga uses models to narrow the possible sequences to a reasonable number of sequences, Jay performs Boolean searches to understand the role of polypeptides and their uses in lubricating joints.

Conclusion

No Claim is allowed

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Andrew Wang, Supervisory Patent Examiner, can be reached at (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

-RSN
18 July 2006

18 July 2006

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER